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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,662	11/21/2003	Sonia Vadrucci	126442-100010-US	1323

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,662	VADRUCCI ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7 and 9-38* is/are pending in the application.

4a) Of the above claim(s) *17-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4,6,7,9-16 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 1/22/07.

Claims 5 and 8 were canceled as requested.

Claims 1-4, 6, 7, and 9-38 remain pending.

Claims 17-37 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/11/06.

Claims 1-4, 6, 7, 9-16 and 38 are under consideration in this Action.

Information Disclosure Statement

An IDS was filed on 1/26/07. The listed references were considered, however, the IDS is not in compliance with 37 CFR 1.98. Most of the citations are incomplete because they lack the title of the journal in which the reference was published, and/or the volume number of the journal. Submission of a corrected IDS is required.

Claim Rejections - 35 USC §/112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6, 7, 9-16 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 6, 7, 9-16 and 38 are indefinite because they recite "the at least two different types of fusion proteins" without proper antecedent basis. Deletion of "types of" is suggested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 7, 9, 11-16 and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to the genus of fusogenic vesicles comprising at least two different viral fusion proteins derived from the viruses selected from the group consisting of VSV, SFV, Sendai, and HIV, wherein the at least two different fusion proteins have different fusion characteristics selected from temperature and pH.

The specification teaches that hemagglutinin (HA) from influenza virus strain X-31 allows fusion at low temperature (e.g. 5°C), whereas HAs from influenza strains PR8/34 or A/Singapore require temperatures of at least 25°C. A search of the prior art indicates that viral fusion activity generally increases with temperature from subphysiological temperatures into the physiological range. The specification discloses no example of any viral fusion protein, other than influenza X-31 HA, that is

distinguished by its sensitivity to temperature. The disclosure of only a single virus fusion protein that is distinguishable from other virus fusion proteins by temperature sensitivity is not considered to be a disclosure of a representative number of species of the genus, and the specification fails to disclose any relevant identifying characteristics of the genus, such as a correlation between structure and function that would imply possession of the genus. Considering the disclosure of the specification as a whole, and the state of the art at the time of the invention, one of skill in the art could not conclude that Applicant was in possession of the claimed genus of viral fusion proteins that are distinguishable from each other by sensitivity to temperature at the time of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7, 9, 11, and 13-16, and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Gunther-Ausborn et al (J. Virol. 74(6): 2714-2720, 2000), as evidenced by Junankar et al (Biochimica et Biophysica Acta, Biomembranes (1986), 854(2), 198-206) and Blough (J. Gen. Virol. 12(3): 317-320, 1971), and Stegman et al (EMBO J. 6(9): 2561-2659, 1987, submitted in the IDS of 1/26/07).

Gunther-Ausborn taught virosome vesicles comprising phosphatidylcholine, phosphatidylethanolamine, and HA trimers from both influenza strains X-47 and A/Shangdong. These HA fusion proteins have fusion properties that are detectable and are distinct from each other. For example, X-47 HA mediates fusion with a pH optimum of 5.1, whereas A/Shangdong HA mediates fusion with a pH optimum of 5.6. See Fig. 1 on page 2715, and paragraph bridging pages 2715 and 2716. The fusion proteins immunologically active substances that are part of the vesicle capsule, and so are considered to be encapsulated. Phosphatidylcholine, phosphatidylethanolamine, are considered to be both liposomal and virosomal lipids because they are components both liposomes and virosomes.

Claims 2 and 15 are included in the rejection because although Gunther-Ausborn was silent as to the lamellarity and size of the virosomes, it was disclosed that they were made by the method of Stegman. The virosomes of Stegman were unilamellar and of a diameter of about 100 nm. Absent evidence to the contrary, the virosomes of Gunther-Ausborn had the same characteristics.

Claims 3 and 4 are included in the rejection because they are interpreted as requiring that the vesicles must be capable of encapsulating the recited substances, not as requiring that the substances must actually be encapsulated in the claimed compositions.

Claim 6 is included because, as evidenced by Junankar, X-47 is distinguished by being sensitive to temperature. It is active only at temperatures above 20°C. As such, it has a "distinct" temperature sensitivity. Note that the rejected claims do not require

that this sensitivity must be "distinct" from the temperature sensitivity of A/Shangdong HA.

Claims 7 and 16 are included because the virosomes bind a cell surface HA-receptor, and so would be specific for cells expressing that receptor. See page 2715, column 2, lines 12-15.

Claims 13 and 14 are included because phosphatidylcholine, phosphatidylethanolamine are known to occur in the envelopes of influenza viruses (see Blough at e.g. Table 2 on page 319), and so are "virosomal lipids" from influenza virus.

Claim 38 is included because the composition of Gunther-Ausborn meets all of the physical limitations of the claim, so the functional limitation of a "pharmaceutical composition" is also considered to be met.

Response to Arguments

Applicants arguments filed 1/22/07 have been fully considered but are unpersuasive. Applicant argues at page 12 of the response that Gunther-Ausborn did not teach encapsulation of a therapeutic substance. This is unpersuasive because the claims allow for encapsulation of an immunologically active substance, and the fusion proteins of Gunther-Ausborn are immunologically active and form part of the vesicle. They are therefore considered to be encapsulated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gunther-Ausborn et al (J. Virol. 74(6): 2714-2720, 2000), in view of Wheeler (US Patent 5,976,567) and taken with the evidence of Junankar et al (Biochimica et Biophysica Acta, Biomembranes (1986), 854(2), 198-206) and Blough (J. Gen. Virol. 12(3): 317-320, 1971).

Gunther-Ausborn taught virosome vesicles comprising phosphatidylcholine, phosphatidylethanolamine, and HA trimers from both influenza strains X-47 and A/Shangdong. These HA fusion proteins have fusion properties that are detectable and are distinct from each other. For example, X-47 HA mediates fusion with a pH optimum of 5.1, whereas A/Shangdong HA mediates fusion with a pH optimum of 5.6. See Fig. 1 on page 2715, and paragraph bridging pages 2715 and 2716. The fusion proteins immunologically active substances that are part of the vesicle capsule, and so are considered to be encapsulated. Phosphatidylcholine, phosphatidylethanolamine, are considered to be both liposomal and virosomal lipids because they are components both liposomes and virosomes.

Junankar provides evidence that X-47 is distinguished by being sensitive to temperature. It is active only at temperatures above 20°C. As such, it has a "distinct"

temperature sensitivity. Note that the rejected claims do not require that this sensitivity must be "distinct" from the temperature sensitivity of A/Shangdong HA.

Gunther-Ausborn did not teach the lipids POPC or DDAB.

Wheeler disclosed a variety of lipids that are routinely used as alternatives in making liposomes. Phosphatidylcholine, phosphatidylethanolamine, DDABl, and POPC was disclosed as an alternatives useful in making liposomes. See column 10, line 39 to column 11, line 32. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). As a result it would have been obvious to one of ordinary skill in the art at the time of the invention to use POPC and/or DDAB to make the vesicles of Gunther-Ausborn.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). The new rejection under 35 USC 102 of claims 2 and 15 is properly made final because it depends on a reference submitted by Applicant in an IDS on 1/27/07,

after the last Office Action. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635